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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,562	07/08/2002	Charles V Clevenger	PENN-0798	7451

7590 12/05/2005

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EXAMINER	
SCHNIZER, HOLLY G	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 12/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,562	CLEVENGER ET AL.	
	Examiner	Art Unit	
	Holly Schnizer	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

The Amendment filed 9/22/05 has been entered. Claims 7-8 are currently pending and have been considered in this Office Action.

Election/Restriction

Applicant's election of Group VII, claims 7 and 8, in the reply filed on 9/22/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Thus, the Supplemental Restriction Requirement as presented in the Office Action mailed 5/18/05, is considered proper and is made FINAL.

Rejection Withdrawn

The rejection of Claims 7-8 under 35 U.S.C. 112, second paragraph as being unclear as to the meaning of "somatolactogenic hormone" is withdrawn in light of Arkins et al. (J. Dairy Sci. 76: 2437-2450) submitted by Applicants, which indicates that prolactin, growth hormone, and placental lactogen are considered somatolactogen hormones (p. 2438, Col. 1, first sentence of second paragraph).

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In the present case, it would require undue experimentation to practice the claimed invention because the Specification does not indicate that cyclophilin B interaction with a somatolactogenic hormone is essential any somatolactogenic function and especially not more than one somatolactogenic function as required by the claims. Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d, 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include (1) quantity of experimentation, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The *nature of the invention* is highly complex. The invention involves the discovery that cyclophilin B interacts with the somatolactogenic hormones, prolactin and growth hormone, that the cyclophilin B can enhance prolactin or growth hormone induced cell proliferation in vitro, and that nuclear retrotranslocation of prolactin into the nucleus is enhanced by cyclophilin B. Prolactin, growth hormone, and placental lactogen are part of a family of hormones called somatolactogenic hormones. The *state*

of the art acknowledges that the specific function of prolactin and growth hormone has remained uncertain (see abstract of Rycyzyn et al. Ann. N Y Acad Sci (2000) 917: 514-521; cited in previous Office Action). Moreover, Arkins et al. (J. Dairy Sci. (1993) 76: 2437-2450) indicate that hormones of the somatolactogen family have many different and unrelated activities some of which are shared by members of the family and some of which are unique to the particular family member (see p. 2438-2443). The present Specification provides *working examples* for production of the cyclophilin B protein, a protein binding assay to detect prolactin-cyclophilin B complexes, use of cell cultures to evaluate the effect of growth hormone or prolactin on cell proliferation, and generation of a cyclophilin mutant lacking amino acids 2-12 of the mature peptide. There are *no working examples* of an assay to identify a compound as an inhibitor of a somatolactogenic function by assessing the ability of the compound to inhibit interaction of cyclophilin B with a somatolactogenic hormone. Moreover, the *guidance* in the Specification involves a discussion of conclusions, drawn from various experiments, which include the following: that cyclophilin B interacts with prolactin and growth hormone (p. 5), that prolactin binds the C terminus of cyclophilin B (p. 5), that cyclophilin A does not interact with prolactin (p. 5), that cyclophilin B and not cyclophilin A enhances the dose dependent growth of cultured cells induced by prolactin or growth hormone (pp. 5-6), that nuclear retrotranslocation of prolactin in cell culture was enhanced by inclusion of cyclophilin B into the medium, and that a mutant cyclophilin B, lacking the putative nuclear localization sequence at the amino terminus, was able to bind prolactin with the same ability as wild-type but did not enhance prolactin induced

proliferation or nuclear retrotranslocation of prolactin. The present claims are drawn to a method wherein the ability of a test compound to inhibit cyclophilin B interaction with any somatolactogenic hormone (claim 7) or prolactin (claim 8) indicates that the test compound will inhibit any somatolactogenic function. However, the present Specification and prior art do not provide evidence that binding of cyclophilin B to a somatolactogenic hormone is essential to any somatolactogenic function. Even the teaching that a mutation in cyclophilin B, deleting the putative nuclear localization sequence, did not affect prolactin interaction with cyclophilin B but did eliminate its ability to enhance prolactin induced proliferation in vitro and nuclear retrotranslocation of prolactin does not provide evidence that cyclophilin B-prolactin binding is essential to these specific activities of prolactin. The Specification does not rule out that cyclophilin B enhances prolactin induced proliferation and nuclear retrotranslocation of prolactin indirectly through interactions of other proteins which affect these activities. The Specification does not provide any experiments which show whether or not a cyclophilin B mutant lacking prolactin (or any other somatolactogenic hormone) binding activity or a compound which inhibits binding would affect a somatolactogenic function (generally) or even in vitro prolactin induced proliferation or nuclear translocation of prolactin (more specifically). Moreover, without guidance as characterization of cyclophilin B-somatolactogenic hormone binding and how this binding affects a given somatolactogenic activity, the affect of an inhibitor of cylcophilin B interaction with one given somatolactogenic hormone on a given somatolactogenic function may not predict with any expectation of success the ability of that inhibitor to affect binding of cyclophilin

B with another hormone or inhibit another somatolactogenic function. Given the high level of complexity of somatolactogenic function, as evidenced by the wide variety of activity these hormones possess and the unique affects each hormone has; the lack of any examples, guidance, or evidence in the Specification or prior art showing that cyclophilin B interaction with a somatolactogenic hormone (generally) or prolactin (specifically) is essential to any particular somatolactogenic function, and the unpredictability of what affect a test compound would have on somatolactogenic function based on its ability to interact with cyclophilin B, it would require one of skill in the art undue experimentation to practice the presently claimed invention. Thus, in summary, the claims are too broad because one of skill in the art would not have any expectation of success in predicting whether or not a test compound would inhibit any somatolactogenic function of any somatolactogenic hormone based on its ability to inhibit that hormone interaction with cyclophilin B. Moreover, the Specification does not provide enablement for testing for the ability of a test compound to inhibit a specific somatolactogenic function based on its ability to inhibit prolactin or growth hormone interaction with cyclophilin B for the reasons stated above. One of ordinary skill in the art would not have an expectation of success in predicting what test compounds would inhibit somatolactogenic functions by determining the compounds ability to inhibit cyclophilin B interaction with a somatolactogenic hormone in the absence of any information regarding the relationship between cyclophilin B-prolactin binding or cyclophilin B-growth hormone binding and a specific somatolactogenic function. Thus, to practice the present invention would not merely require a repetition of what is

described in the specification but it would require a characterization of the relationship between cyclophilin B-somatolactogenic hormone binding and each of the multitude of somatolactogenic functions (some of which are unique to a given hormone and each of which is independent of the others). It is this characterization, which would be required to carry out the claimed invention with any expectation of success and without trial and error that is considered undue experimentation.

Conclusions

No Claims are allowable. This action has not been made final due to the new rejection which raises new issues.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-0958. The examiner can normally be reached on Tuesday-Thursday from 10 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Holly Schnizer
December 1, 2005